CHAPTER I

GENERAL INTRODUCTION

The field of Coordination Chemistry is now the most active research area in Inorganic Chemistry encompassing a great variety of subjects and phenomena. About seventy percentage of the papers appearing in Inorganic chemistry journals in recent years deal with various aspects of coordination compounds which play important roles in applied science and industry. The involvement of metal ions in biological processes and the role of metal complexes in biological systems have culminated in the emergence of a new branch viz. Bio-inorganic chemistry. Coordination complexes serve as dioxygen carriers in oxygen activators and nitrogen carriers in nitrogen fixation. Metal chemotherapy and chelation therapy have now drawn attention as additional outlets for coordination chemistry. The nutritional and pharmacological aspects of coordination complexes have been reviewed¹.

The development in the field of coordination chemistry dates back to French Revolution. During that period several dyes were isolated which were later found to be typical coordination compounds. The modern study of metal complexes begins with the work of two men, Alfred Werner and
Sorphus Mads Jorgensen. Early workers identified coordination compounds of only a few metals and with common coordination number such as four and six. More recent research activities are concerned with complexes of nearly all the metals in the periodic table in their many oxidation states and with all possible coordination numbers from two to twelve. Reason for this advancement can be attributed to the formulation of excellent theories of electronic structure of metal ions in coordination compounds such as ligand field and molecular orbital theories and the availability of modern sophisticated instruments which are powerful tools for structure determination.

The condensation product of primary amines with carbonyl compounds was first reported by Schiff and the products are often referred to as Schiff bases. Schiff bases contain azomethine group, \(-RC=\text{N}\)-. The synthesis and properties of Schiff bases have been widely reviewed. Various studies have shown that the presence of a lone pair of electrons on triagonally hybridised nitrogen atom of \(=\text{C}=\text{N}\)-group is of fundamental chemical and biological importance. For the relative easiness in the synthesis and also for the synthetic flexibility, Schiff base with widely varying substituents can be obtained by proper choice of reactants. By changing the nature and position of the donor atoms and groups, it is possible to control the size of
chelate ring formed and to exploit the effect of substitution. Due to all these factors Schiff bases find application in many fields of fundamental and applied research.

Metal complexes derived from Schiff bases have been known for over one hundred and fifty years. The systematic study of Schiff base complexes by Pfeiffer and coworkers inspired the chemists during the last four decades. There have been a prodigious growth of the published literature including a few excellent reviews. The general procedures employed for the synthesis of Schiff base complexes are given below.

1. Reaction of metal ion and Schiff base in a suitable solvent.
2. Reaction of metal ion and Schiff base in presence of added base such as acetate or hydroxide.
3. Reaction of an amine with a preformed complex of aldehyde.
4. Addition of an aldehyde to a metal amine complex (template reaction). This method has been used for the preparation of complexes of Schiff bases of diamines.

The availability of different types of amines and carbonyl compounds enabled the synthesis of Schiff bases of diverse structural features. Nevertheless, most of the
studies are on metal complexes of schiff bases derived from salicylaldehyde\textsuperscript{14}. The presence of phenolic OH group sufficiently near to the azomethine group of salicylidimines makes them versatile multidentate ligands complexing with almost all metal ions.

Studies on schiff base complexes of copper(II) are, as ever, popular. An excellent review of both conformation and interconversion of Cu(II) complexes has appeared\textsuperscript{19}. Copper(II) ion has been reported to form stable complexes with the tridentate schiff bases, salicylidiminoalkylpyridines\textsuperscript{20}. Abnormally low magnetic moment values were shown by Cu(II) complexes of biologically active schiff bases of salicylaldehyde with L-methionine and L-leucine and amino sugars\textsuperscript{21,22}. Copper(II) complexes with apically coordinated thioether group of ligands derived from salicylaldehyde or pyridine-2-aldehyde and 1,2 diamino, 5-thiahexane have been proposed to have five coordinate geometry by their ESR spectral studies\textsuperscript{23}. Syamal and coworkers have synthesised a large number of cobalt(II), iron(III) and oxovanadium(IV) complexes with tridentate ligands derived from o-aminobenzylalcohol and salicylaldehyde or substituted salicylaldehyde. The cobalt(II) complexes exhibit abnormally low magnetic moments at room temperature ($\mu_{\text{eff}}=0.98-1.48 \text{ BM}$) suggesting dimeric structure with oxygen of the alcohol as the bridging atom.
Similar five coordinate oxygen bridged dimeric structure was proposed for iron(III) complexes\textsuperscript{24-26}. Syamal and Kumar have reported eight coordinate dihydroxozirconium(IV) complexes of monovalent tridentate Schiff bases derived from 2-aminoethanethiol and salicylaldehyde or 2-hydroxynaphthaldehyde\textsuperscript{27}.

Complexes of N-salicylidene-2-aminopyridine with Cu(II), Co(II) and Ni(II) are interesting in that the ligand acts as neutral bidentate one coordinating with its azomethine nitrogen and phenolic oxygen without deprotonation. But the ligands, N-(4-hydroxybenzylidene)-2-aminopyridine and N-(4-hydroxy-3-methoxybenzylidene)-2-aminopyridine have been reported to coordinate to Cu(II), Co(II) and Ni(II) through their pyridine nitrogen atom\textsuperscript{28}. The structural studies of the eight coordinate chelate, bis(NN'-disalicylidene-1,2-phenylene dianimato)cerium(IV) have revealed that the ligands in the complex have sandwich orientation and the trapezoidal planes intersect at 88.2°\textsuperscript{29}. The electrochemical behaviour of a series of mono and binuclear complexes of dioxouranium(VI), nickel(II) and copper(II) with Schiff base derived from 3-formyl salicylaldehyde and 1,2-diaminoethane has been investigated. This potential hexadentate compartmental ligand exhibits an outer $O_2O_2$ and an inner $N_2O_2$ coordination. The redox potentials of metal ions in these two different and adjacent
chambers were investigated and compared with those of analogous complexes of the ligand derived from o-acetylphenyl and 1,2-diaminoethane\textsuperscript{30}.

An investigation on the magnetic susceptibilities at varying temperature (90-295K) of iron(III) complexes with several quadridentate Schiff bases derived from salicylaldehyde and diamines has led to the classification of these complexes into four types viz., high spin (\(S=5/2\)), low spin (\(S=1/2\)), intermediate spin (\(S=3/2\)) and cross over complexes and the last of which have a ligand field strength near the cross over point of high-spin and low-spin types. From ESR studies, the existence of a spin equilibrium was established for the cross over complexes\textsuperscript{31}. Similar spin equilibrium was shown by iron(III) complexes of unsymmetric quadridentate Schiff bases of ethylenediamine in solution\textsuperscript{32}. Sharma et al. have investigated the ESR spectra of bis (N-allyl salicylidiminato) copper(II) monohydrate and similar complexes in an X-band ESR spectrometer (fabricated) and evaluated the influence of distortion in symmetry around Cu(II) ion caused by substituted groups on Spin-Hamiltonian parameters\textsuperscript{33}.

The Schiff bases derived from 2-hydroxy-acetophenone and 2-hydroxy,1-naphthaldehyde with various amines are potential chelating agents. Patel and Patel have reported the synthesis and spectral studies of Cu(II)
complexes of the tridentate Schiff bases derived from 2-hydroxyaniline and 2-hydroxyacetophenone or substituted hydroxyacetophenone. Spectral studies of 1-(o-hydroxyphenylimino methyl)-2-naphthol with 3d metal ions have established dimeric square planar structure with phenolic oxygen bridging. Dave et al. were successful in synthesising and characterising octahedral complexes of Cr(III), Fe(III) and Co(III) with the Schiff base bis (2,5-dihydroxyacetophenone) ethylenediamine and square planar or tetrahedral complexes of Cu(II) and Ni(II) with bis (2,5-dihydroxyacetophenone) ethylenediamine.

Biologically active Schiff bases derived from 5-methyl,2-hydroxyacetophenone and glycine has been reported to show chelating behaviour towards copper(II), cobalt(II) and oxovanadium(IV) ions to give neutral complexes with square planar, tetrahedral and square pyramidal geometries respectively. Recently, Mahapatra et al. have synthesised complexes of divalent copper, nickel, iron, cobalt, zinc and mercury with the Schiff bases, 2-hydroxyacetophenone glycine and 2-hydroxyacetophenone alanine. IR, electronic and ESR spectral and DTA studies of these complexes reveal dimeric structure except for zinc and mercury complexes. It has been reported that the template condensation of $[\text{Ni(NH}_3\text{)}_4]^{2+}$ with 2-hydroxyacetophenone, 2-hydroxy-naphthaldehye and salicylaldehyde invariably yields
corresponding imine complexes\textsuperscript{41}.

The schiff bases formed by the condensation of $\beta$-ketoaldehydes or $\beta$-diketones with p-amines are closely related to salicylidimines. In $\beta$-ketoamine complexes, the donor pair is ON as in the case of salicylidimines. The literature on $\beta$-ketoamine complexes is much less extensive than that of salicylidimine complexes. Complexes of $\beta$-diketones have remained a topic of active research for close to one hundred years. Their schiff base derivatives have received only very little attention while the salicylaldehyde analogues have been extensively studied$^{14}$. Tetradentate schiff bases derived from acetylacetone and m-, p- and o-phenylenediamines and their complexes with first row transition metal ions have been synthesised and characterised. Most of the complexes exist as dimers. ESR spectra of copper(II) and oxovanadium(IV) complexes reveal considerable metal-metal interaction$^{42,43}$.

The schiff bases derived from heterocyclic aldehydes such as furan-2-aldehyde, thiophene-2-aldehyde and pyridine-2-aldehyde have been found to act as potential ligands and show considerable antibacterial activity\textsuperscript{44-49}. In many of the complexes reported of the ligands, the heteroatom enters into coordination with metal ions. The ESR spectrum of bis(thiophene-2-carboxaldehyde)-o-tolidin complex of Cu(II) shows a compressed rhombic symmetry with a
distorted triagonal-bipyramidal geometry having $d_{2}^2$ ground state. Thiophene-2-aldehyde-2-quinolylhydrazone and thiophene-2-aldehyde-2-benzothiazolylhydrazone have been used for spectrophotometric determination of microgram quantities of vanadium(V) and copper(II) respectively. Work on the complexing nature of oximes of furfural and thiophene-2-aldehyde reveals that the oximes can behave either as univalent monodentate or neutral bidentate ligands.

Complexes of schiff bases have been reported to act as selective catalyst. The autooxidation of cumene has been catalysed effectively by transition metal complexes of N-salicylidene-o-aminophenol. Many of the copper(II) schiff base complexes exhibit liquid crystalline nature. The square planar copper(II) complex of PP'-disubstituted salicylidene anil showed liquid crystal transition at higher temperature than the ligand. ESR spectral studies were helpful to determine the structural organisation of smectic-phase state of the schiff base-Cu(II) complex. An isotropic phase was observed at about 161°, a smectic A-phase at 153-161 and smectic C-phase at 135-153°C. A stable texture phase was found to appear only below 135°C. The investigations on the possibility of using metal complexes of schiff bases themselves as potential ligands have been reviewed. Lanthanides have been reported to form stable complexes with...
the chelate, N,N'-1,3-propanediylbis(salicylidenediminato) copper(II) which acts a tridentate ligand\textsuperscript{60}.

A brief review on the metal complexes of Schiff bases derived from Isonicotinic acid hydrazide, Salicylic acid hydrazide and o-Aminothiophenol

The Schiff bases derived from acid hydrazides, known as hydrazones are azomethines having general formula RCH=N-NH-R' (R=alkyl, aryl or heteroaryl., R'=acyl, aroyl or heteroaroyl) and are distinguished from other members of this class by the presence of two interlinked nitrogen atoms. These hydrazones can behave as bidentate coordinating through keto oxygen and azomethine nitrogen atoms. They can function as polydentate ligands when one or more coordinating functionality is present in the proximity of nitrogen or oxygen atom.

Most of the aroyl and heteroaroyl hydrazones are slightly coloured solids. Several aroyl hydrazones especially 4-nitro and 2,4-dinitro derivatives have well defined crystalline structures with sharp melting points. Being readily available, hydrazones find wide application in the synthetic chemistry for the preparation of compounds of most diverse structure and in analytical chemistry for the identification or isolation of carbonyl compounds and also
for the detection of large number of cations. Their applications have also been reported as plasticisers, stabilizers for polymers, polymerisation inhibitors, antioxidants etc. However, the most valuable property of hydrazones is perhaps their high physiological activities. Many of these compounds are used in the treatment of tuberculosis, leprosy and mental disorders. Metal complexes derived from these hydrazones have been characterised and put into diverse use.

**Metal complexes of isonicotinoylhydrazones**

4-Pyridine carboxylic acid hydrazide, isonicotinoylhydrazine, having high specific activity against tuberculosis has been known under a number of names (isoniazid, isonex, neotaben, tubazid, dinacrin etc.)\(^6^5\). The ability of isoniazid to condense with aldehydes and ketones to give well defined crystalline schiff bases, hydrazones with sharp melting points has been made use in the identification of isoniazid even in pharmaceutical preparations. The schiff bases derived from isoniazid exhibit antitubercular activity equal to that of isoniazid itself\(^6^2,6^6\). However continuous administration of isoniazid can cause, peripheral neuritis, a dose-related effect likely to occur in malnutritioned individuals and chronic
alcoholics\textsuperscript{67}. Wood and Kurylo have investigated the effect of isonex on the amino acid contents of nerve endings (synaptosomes) in different region of rat brain\textsuperscript{68}. The detoxification of metals in animal body by administering chelating agent in controlled doses is referred to as chelation therapy. Isonex has been applied successfully to control the copper and cobalt contents in rabbit's liver during the period of experimental tuberculosis\textsuperscript{69}. The therapeutic use of isoniazid has so advanced that the membrane coated controlled release isonex tablets acting with zero order kinetics have been prepared\textsuperscript{70}.

The coordination compounds of isonicotinoyl hydrazine with metal ions have been well investigated\textsuperscript{71-73}. In most of the complexes reported of isoniazid, it acts as a neutral bidentate ligand coordinating through its amino nitrogen and carbonyl oxygen atoms. However, X-ray and IR spectral studies of zinc and cadmium iodide and thiocyanate complexes of isoniazid have suggested coordination through pyridine ring nitrogen atom\textsuperscript{74}. The complexes of isonex with Cu(II), Ni(II), Co(II) and Zn(II) have been investigated as cytotoxic agents \textit{invitro} against HS/5 and KB tumours\textsuperscript{75}. Aggarwal et al. have synthesised and characterised complexes of N-benzoyl and N-acetyl derivatives of isoniazid with divalent copper, nickel, cobalt, zinc and manganese and oxovanadium(IV) ions. IR spectral studies of the complexes
reveal that N-benzoyl, N'-isonicotinoylhydrazine acts as a univalent bidentate ligand and the probable bonding sites are enolic oxygen arising from the enolisation of keto group attached to the pyridine ring and nitrogen of NH group. However, N-acetyl N'-isonicotinoylhydrazine behaves as bivalent quadridentate ligand forming square planar complexes with Cu(II) and high spin octahedral complexes with Mn(II), Ni(II) and Co(II) ions. The IR and Mossbauer spectral studies of iron(II) thiocyanate complex of isoniazid have supported the neutral bidentate character of isoniazid as chelating agent. The derivative diacetyl bis (isonicotinoylhydrazone) was successfully used as reagent for the spectrofluorometric determination of zirconium(IV) in ppb quantity.

Metal complexes of the schiff base derived from isoniazid have been well investigated. N-salicylidene N'-isonicotinoylhydrazine used as a metallochromic indicator forms stable complexes showing invitro antitubercular activity. This ligand has four potential donor sites viz. heterocyclic nitrogen, azomethine nitrogen, carbonyl oxygen and phenolic oxygen atoms and a large number of complexes have been reported. Prabhakaran et al. have investigated extensively the ligand function and substrate effect on M-O stretching frequency in some dioxomolybdenum(VI) complexes of schiff bases derived from
isoniazid and salicylaldehyde or 2-hydroxynaphthaldehyde. Gopinathan et al. reported stable monomeric penta-coordinated complexes of ruthenium of formula $[\text{Ru}(\text{PPh}_3)_2\text{L}]$, ($\text{H}_2\text{L} = \text{schiff base derived from isoniazid and salicylaldehyde or } \beta$-diketones). The complexes absorb carbon monoxide to form six coordinated complex, $[\text{Ru}(\text{PPh}_3)_2\text{L(CO)}]$ and the schiff bases coordinate to Ru as dibasic tridentate.

Teotia et al. have synthesised trivalent chromium, manganese and cobalt complexes of 2-hydroxyacetophenone isonicotinoylhydrazone and characterised by IR and electronic spectra and magnetic measurements. The ligand field parameters of metal ions revealed distorted geometry for the complexes. They extended their work to isolate and characterise the dimeric four coordinated complexes of 2-hydroxyacetophenone isonicotinoylhydrazone with Pt(II), Pd(II) and Cu(II) in which the ligand exhibits bivalent tridentate nature with the deprotonated enolic oxygen as the bridging atom. The open chain tetradentate schiff base containing two azomethine groups, acetylacetone bis (isonicotinoylhydrazone) has been reported to form stable complexes with trivalent chromium, manganese and cobalt and dioxouranium(VI) and oxo and hydroxovanadium(IV) ions.

Acetone isonicotinoylhydrazone complexes of divalent ions of 3d metals and dioxouranium(VI) have been
reported. In these complexes, the hydrazone acts as neutral or monobasic bidentate or tridentate\textsuperscript{91-93}. Singh et al. synthesised divalent metal complexes of the schiff base derived from isoniazid and pyridine-2-aldehyde and pyridine-4-aldehyde and characterised by IR, electronic, ESR and NMR spectra. ESR spectral studies of Cu(II) complexes show that the unpaired electron is in the $d_{x^2-y^2}$ orbital of copper(II) ion. Pyridine-4-aldehyde isonicotinoylhydrazone and its Co(II), Ni(II) and Zn(II) complexes show good antibacterial activity against \textit{S. aureus}, and \textit{E. coli}\textsuperscript{94,95}. Metal complexes of the schiff bases derived from isoniazid and anisaldehyde and benzoyl pyridine have been synthesised and characterised\textsuperscript{96,97}. Thermochemical analyses of solid complexes of isonicotinoylhydrazones of a number substituted benzaldehyde prepared in neutral and basic media have been reported\textsuperscript{98}. Recent investigation on the Mossbauer spectra of iron(III)chloride complexes of isonicotinoylhydrazones derived from a number of carbonyl compounds by Jain et al. ascertained high-spin weak ligand field octahedral microsymmetry of ligands around Mossbauer atom\textsuperscript{99}.

**Metal complexes of salicyloylhydrazones**

Salicyloylhydrazine, o-hydroxy benzoic acid hydrazide is a well known antibacterial and antifungal
agent. Apart from the biological activity, salicyloylhydrazine has analytical and technological importance. Salicyloyl hydrazine has been successfully used as a reagent for the spectrophotometric estimation of iron in copper alloys\textsuperscript{100}. The use of salicyloylhydrazine and aryl substituted derivatives as antioxidant and stabilizers for fats, oils, polymers etc has been reported\textsuperscript{101}.

The presence of a phenolic OH group near the carbonyl group in salicyloylhydrazine makes it a potential monovalent or neutral NOO donor coordinating through the amino nitrogen, carbonyl oxygen and phenolic oxygen with or without deprotonation. Numerous stable complexes of salicyloylhydrazine with transition metals and rare earths have been synthesised, characterised and put into diverse use. The spectrophotometric investigation of salicyloylhydrazine with tetravalent metal ions has been reported\textsuperscript{102}. Extensive studies on the complexes of divalent 3d metal and lanthanone salts with salicyloylhydrazine have shown that the ligand acts as a neutral bidentate one, coordinating through its carbonyl oxygen, and amino nitrogen atoms\textsuperscript{103-107}. However, in basic medium salicyloylhydrazine acts as a monobasic tridentate towards divalent Cu, Zn, Co and Fe\textsuperscript{108}. Narang et al. have synthesised neutral aquo complexes of N-salicyloylhydrazine and NN'-disalicyloyl hydrazine with divalent metal ions\textsuperscript{109}. Bis(salicyloylhydrazine)nickel-
dipyridinate has been used as good light stabilizers for polymers$^{110}$.

The metal complexes of salicyloylhydrazones, the schiff bases derived from salicyloylhydrazine and carbonyl compounds are of great importance in many fields of fundamental and applied research. N-salicylidene,N'-salicyloylhydrazine is the one which is extensively studied as the potential ligand as it can exist in keto or enol form. The complexes of divalent metal ions with N-salicylidene, N'-salicyloylhydrazine and N-(3-hydroxy, 2-naphthylidene) N'-salicyloylhydrazine have been synthesised and characterised by elemental analysis and IR, electronic, ESR and NMR spectral and magnetic studies. Both the ligands in their enol form act as bivalent tridentate OON donors. The former ligand uses the oxygen atoms of deprotonated phenolic group of hydrazide part and enolic group and nitrogen atom of azomethine group for coordination leaving phenolic group of aldehyde part uncoordinated$^{111}$ whereas the latter one coordinates through the oxygen atoms of deprotonated phenolic group of naphthylidene part and enolic group and the nitrogen of azomethine group leaving phenolic group of hydrazide non coordinated. All the complexes are dimeric through oxobridge with considerable metal-metal interaction. The morphology of the complexes of N-(3-hydroxy-2-naphthylidene)N'-salicyloylhydrazine is revealed
by Transmission Electron Microscopic Studies\textsuperscript{112}.

The investigations of Temerk et al. on the chelating ability of N-salicylidene,N'-salicyloylhydrazine to nitrate and sulphate of copper(II) proved that the ligand can function as a neutral bidentate coordinating through the carbonyl oxygen and azomethine nitrogen atoms in its ketoform\textsuperscript{113}. Dioxouranium(VI), oxomolybdenum(VI), organooxytitanium(IV) and organotin(IV) derivatives of N-salicylidene,N'-salicyloylhydrazine have been synthesised and well characterised\textsuperscript{114-116}. The magnetic and ESR studies of o-hydroxypropiophenone salicyloylhydrazone copper(II) complex have revealed a dimeric structure for the complex with antiferromagnetic interaction. A super exchange pathway via the oxygen atom has been proposed\textsuperscript{117}.

The synthesis and characterisation have been reported of complexes of the type M(HL)\textsubscript{2}, FeLCl, Fe(H\textsubscript{2}L)SO\textsubscript{4}H\textsubscript{2}O and M(HL)ClnH\textsubscript{2}O [H\textsubscript{2}L=R-C\textsubscript{6}H\textsubscript{4}-CH=N-NH-C\textsubscript{6}H\textsubscript{4}OH(o), R=H, 3-OMe, 5Cl, 5Br, 5Me and 5NO\textsubscript{2} and M(\textsubscript{n})=Co(\textsubscript{2}), Ni(\textsubscript{2}), Cu(\textsubscript{1}) and Pt(\textsubscript{1})]. Extensive studies show considerable antiferromagnetic interaction in FeLCl with the exchange parameter, J nearly 8.0 cm\textsuperscript{-1}. Mossbauer spectrum of FeLCl shows symmetric quadrupole doublet splitting and the symmetry is temperature dependent and at low temperature symmetric split is obtained. ESR study shows that Cu(II) complex is square planar with d\textsubscript{x}^2-y^2 ground state. The
complexes exhibit more antitumour activity than the corresponding ligands\textsuperscript{118}.

Datta and Pal have investigated the retention or abstraction of metal-oxobonds during the reaction of salicyloylhydrazine with acetylacetone of oxovanadium(IV), cis-dioxomolybdenum(VI) and trans-dioxouranium(VI). IR and electronic spectral studies reveal that unlike the reactions reported of salicyloylhydrazine and bis(acetylacetonato)-oxovanadium(IV) and bis(acetylacetonato)(cis-dioxo)molybdenum(VI), no abstraction of trans uranyl-oxobonds occurred in the reaction of salicyloylhydrazine with bis(acetylacetonato)(trans-dioxo)uranium(VI), but resulted in the formation of mixed ligand complex of dioxouranium(VI) with acetylacetone and schiff base, acetylacetone salicyloylhydrazone\textsuperscript{119,120}. The spectral and magnetic studies reported of Mn(II) complexes of the schiff base derived from salicyloylhydrazine and various $\beta$-diketones revealed tetrahedral geometry for the complexes\textsuperscript{121}. Acetone salicyloylhydrazone has been reported to act as univalent tridentate towards divalent Cu, Ni, Co and Zn and neutral bidentate towards UO$_2$SO$_4$.\textsuperscript{122,123}

Salicyloylhydrazones of heterocyclic aldehydes are of current interest as potential ligands possessing antibacterial activity. N-Furyldene,N'-salicyloylhydrazine complexes of the general formula [ML$_2$]Cl$_2$H$_2$O (M = Cu, Ni,
Co, Mn, Cd or Zn., L=N-furylidene,N'-salicyloylhydrazine) have been synthesised and characterised. The ligand acts as neutral bidentate one coordinating through its carbonyl oxygen and azomethine nitrogen atoms\(^{124}\). The schiff base, pyridine-2-aldehyde salicyloylhydrazone has been reported to act as monobasic tridentate towards Zn(II), Cd(II) and Hg(II) forming octahedral complexes. The X-ray spectral study of Zn(II) complex reveals monoclinic space group \(\text{C}_2\text{h}\) and the ligand sites are located from \(\text{H}^1\) and \(\text{C}^{13}\) NMR spectra of the complexes\(^{125}\). 2-Benzoylpyridine salicyloylhydrazone has been reported to act as monovalent tridentate NNO donor towards divalent Cu,Ni,Co,Mg,Zn,Cd and Hg and tin(IV) and dioxouranium(VI)\(^{126}\).

Pelizzi et al. have synthesised and characterised Sn(IV) and Fe(III) complexes of 2,6-diacetylpyridine bis(salicyloylhydrazone)\(^{127}\). Mossbauer and X-ray spectral techniques have been employed to investigate the geometry of the Fe(III) complex\(^{128}\). Abnormally low magnetic moments have been reported for octahedral nickel(II) and square planar copper(II) complexes of glyoxal bis(salicyloylhydrazone). The low magnetic moment of Cu(II) complex is attributed to the strong antiferromagnetic interaction between interacting Cu(II) ions and that of Ni(II) complex to several other factors affecting the stereochemistry\(^{129}\).

Iskandar et al. have synthesised a number of
Co(II) and Ni(II) complexes with various salicyloylhydrazones and characterised by elemental analysis and IR, electronic and other spectral studies\textsuperscript{130,131}. Agarwal et al. evaluated the ligand field parameters of Ni(II) and Co(II) ion under the influence of the ligand N-vanillidene, N'-salicyloylhydrazine in complexes\textsuperscript{132}.

The complexing ability of salicyloylhydrazones has been extensively used in analytical chemistry. Spectrophotometric estimation of vanadium at ppb level is made possible by pyridine-2-aldehyde salicyloylhydrazone\textsuperscript{133}. Pyrochatachol-3-aldehyde salicyloylhydrazone is used as the reagent for fluorometric estimation of zinc in ppb level\textsuperscript{134}.

**Metal complexes of schiff bases derived from aminothiophenols**

Thiols are organic molecules having SH group often called mercapto group\textsuperscript{135}. The hydrogen atom of thiophenol group shows higher reactivity in comparison with its hydroxyl counterpart, invariably due to the large atomic size of sulphur, longer SH bond length and smaller bond energy\textsuperscript{136}. Thiol groups occur in large number of biological systems. Thiols also play important role in the manufacture of insecticide and pharmaceuticals as sulfonal and trimol (ethanethiol)\textsuperscript{137}.

The presence of NH\textsubscript{2} group near SH enhances the
biological and chemical activity of thiols. Chemisorption of 4-aminothiophenol on iron wire has been proved to inhibit corrosion\textsuperscript{138}. Aminothiols, their derivatives and metal complexes are of great interest due to their well known carcinostatic and antiviral activity. As sulphur donor ligands can produce more effective M-L overlap in comparison to oxygen donors, stronger M-L bonds result\textsuperscript{136}.

o-Aminothiophenol and o-methylthiobenzenethiol have been reported to form square planar complexes with Ni(II), Pd(II) and Pt(II) and the Pd(II) complex reacted with \( K_2[\text{PdCl}_4] \) to give thiolobridged complexes which showed greater stability than the reported chlorobridged complexes\textsuperscript{139,140}. 2-Aminothiophenol can be considered as a border line ligand which can coordinate to both Cu(II) and Cu(I) and it is a suitable ligand for building up more complicated systems that may act as biological model\textsuperscript{141}.

The condensation of o-aminothiophenol with carbonyl compounds does not normally lead to the isolation of corresponding schiff base, but thiazoline or benzothiazoline is mostly obtained\textsuperscript{142,143}. However, in presence of metal ions, the cyclic thiazoline or benzothiazoline rearranges to give expected schiff base-metal chelate quantitatively\textsuperscript{144-146}. The schiff base, salicylaldehyde o-aminothiophenol is the one which is extensively studied as the potential ligand derived from
o-aminothiophenol. It can function as a bivalent tridentate to form 1:1 dimeric chelates with divalent metal ions. Theriot et al. have been successful in the isolation of o-aminothiophenol derivatives of salicylaldehyde and 2-hydroxynaphthaldehyde and synthesis of complexes of those schiff bases with Cu(II) and VO(IV) ions. Most of the complexes show abnormally low magnetic moments at room temperature. The measurements of magnetic moment at three different temperatures show the presence of antiferromagnetic exchange due to metal-metal interaction\textsuperscript{147}.

Sharma et al. have reported the synthesis, characterisation and antibacterial activity of mono nuclear complexes of the formula \([\text{M(H}_2\text{L)}n\text{H}_2\text{O}] (\text{H}_2\text{L}=\text{N-salicylidene-o-aminothiophenol.}, \ n=1 \text{ for M=Ni, Cu and } n=3 \text{ for M=Co, Mn or Zn}). \) The antibacterial activity of the ligand is found to increase on chelation\textsuperscript{148}. \text{N-Salicylidene-o-aminothiophenol} has been reported to form mixed ligand complexes with Ti(IV) alkoxides. The complexes are either monomeric six or five coordinate. IR, electronic, NMR and mass spectral studies have indicated that the ligand in the form of benzothiazoline rearranges to schiff base in Ti(IV) complexes\textsuperscript{149}. The metal technetium and its compounds are technologically valuable and technetium complexes of equal status have been prepared. Pietzsch et al. reported lipophilic technetium(V) complexes obtained by the action of
Tc(V)glucosate with schiff base derived from salicylaldehyde and o-aminothiophenol, aminoethanethiol or \(\alpha\)-amino \(\beta\)-thiol propanoic acid. The complexes show radio chemical purity and the existence of lipophilic technetium complexes is proved by high voltage electrophoresis\(^{150}\). The mixed oxotechnetium(V) complexes of N-salicylidene-o-aminothiophenol and thiophenol or mercaptocarboxylic acid have been synthesised and characterised recently\(^{151}\). The method of substoichiometric determination of Sn(IV) in organotin compounds found in coal fly ash by coordination with N-salicylidene-o-aminothiophenol in non-aqueous medium has been reported to have high commercial importance\(^{152}\).

The condensation product of o-aminothiophenol and heterocyclic aldehydes has been reported to give typical schiff base complexes with divalent metal ions\(^{153-155}\). Tandon and coworker have reported Pd(II) complexes of varying composition such as Pd(HL)Cl\(_2\), Pd(HL)\(_2\)Cl\(_2\) and PdL\(_2\) (HL=condensation product of o-aminothiophenol and furfural, pyridine-2-aldehyde or thiophene-2-aldehyde). IR and NMR spectra of these complexes reveal coordination through azomethine nitrogen and sulphur of thiol and the electronic spectra suggest square planar structure\(^{156}\). Tayim and Saleemath reported the formation of normal schiff base complexes of divalent metal ion with 2-thiazolin-2-ylthiophene isolated from o-aminothiophenol and 2-thiophene aldehyde\(^{157}\).
Condensation of 3-aminothiophenol with carbonyl compound gives normal schiff base. Syamal et al. have synthesised complexes of N-salicylidene-3-aminothiophenol with oxovanadium(IV), copper(II) and dioxouranium(VI) ions\textsuperscript{158,159}. Copper(II) complexes exhibit low magnetic moments at room temperature and significant decrease on lowering the temperature. This has been attributed to antiferromagnetic effect or to the influence of spin-orbit coupling of the ground state for a spin doublet species. The exchange integrals, $J$ of the complexes are negative and in the range 203-325 cm\textsuperscript{-1} indicative of the presence of antiferromagnetic exchange interaction with an $S=0$ ground state\textsuperscript{160}. The metal chelates of o-aminothiophenol and its schiff base with benzaldehyde have been found to influence the oxidation of cumene by inhibiting the acceptors of cumene peroxide radical\textsuperscript{161}.

Antimicrobial activity of metal complexes

Most of the microorganisms acquire resistance to common antibiotics. Retention of potency of antibiotic drugs will be highly desirable in clinical treatments. Metals, especially transition metals and lanthanides, are found fatal to microorganism but not to the host in microquantities. Metal complexes of biologically active organic compounds and
their derivatives have been tested for the effectiveness as antibacterial, antiviral, antitubercular, antifungal and anticancer drugs. Active research in this field of microbiology has been commenced only two decades ago.

In the present investigation of antibacterial assay of transition metal complexes, the microorganism used is *Staphylococcus aureus*. Hence, this part of the review is confined mainly with earlier studies on antistaphylococcal activity of various organic compounds and their metal complexes.

*Staphylococcus aureus* is a common and versatile pathogenic microorganism belonging to the genus *staphylococcus* consisting of cluster forming gram-positive cocci. Most of the strains form golden pigmented (*aureus*) colonies, some form white or cream coloured colonies *Staphylococcus* is the cause of wide range of different kinds of major and minor pyogenic infections, some are harmless as the commensal parasite in the anterior nares and on moist areas of skin in 20 to 30 percentage of healthy persons. The number of their cell components, soluble toxins and non-toxic aggressins, including coagulase, contribute to the ability of *S. aureus* to over come the body's defences and to invade, survive in and colonize the tissues. When ingested in food, commonly cooked meat, in which *Staphylococcus* has been growing profusely, the enterotoxin causes nausea,
vomiting and diarrhoea within six hours (Staphylococcus food poisoning)\textsuperscript{162,163}.

Most strains of \textit{S. aureus} acquire resistance to common antibiotic drugs. When penicillin first came into wide use no resistant strain were found in a study of 29 clinical isolates of \textit{S. aureus} obtained in 1942. However, an increasing proportion of \textit{S. aureus} strain isolated from patients were later found to be resistant to penicillins. The growing incidence of resistance of \textit{S. aureus} was accompanied by more frequent problems with antibiotic resistance in other organisms as well\textsuperscript{164}. The stereospecific derivatives of antibiotics and their metal salts are being administered to overcome this crisis. Spiramycin methylphenylhydrazone has been found to be the most potent inhibitor of \textit{S. aureus} growth compared to other hydrazones of spiramycin\textsuperscript{165}. Ethylenediaminetetra acetate (EDTA), 8-hydroxyquinoline and o-phenanthroline have been reported to suppress the intrinsic resistance of several isolates of \textit{S. aureus} to methicillin, benzyl penicillin, cephalothin and cephaloridine. But addition of metal ions reversed the effect of above chelating agents. Ca(II), Mn(II), Ni(II), Fe(II) and Cu(II) show the most adverse effect with EDTA and Ni(II) ion shows the same effect with o-phenanthroline\textsuperscript{166}.

Azomethines are reported to show greater tuberculostatic and bacteriostatic effect than the
corresponding aldehydes and ketones \(^62,167-169\). However, isonicotinoylhydrazine has shown a decrease in the antibacterial activity on forming derivatives by replacing aminohydrogens \(^170\). Arylsulphonylhydrazones of a few heterocyclics remained non-active against \textit{S. aureus} \(^171\). The effect of substituents on antibacterial activity of \(p\)-substituted phenyl carbamic acid against \textit{S. aureus} has been extensively studied to derive a molecular structure-activity relationship. The compounds with substituent \(OC_5H_{11}\) or \(C_6H_5CH_2O\) showed high antistaphylococcal activity while those with \(CO.C_6H_5\), \(OCH_3\) or \(OC_2H_5\) showed least activity \(^172\).

Salicylic acid and its derivatives are well known for their antimicrobial activity. Salicylic acid and 3,5-dinitrosalicylic acid are reported to show increased antistaphylococcal activity on coordination with Cu(II), Ni(II), Co(II), Mn(II), Fe(II), Zn(II) and oxovanadium(IV) ions \(^173,174\). Chathopadyaya has investigated the relationship between the structure of metal salicylates in solution and their antibacterial activity \(^175\). 8-Hydroxyquinoline and its derivative used as ingredients of many pharmaceutical preparations have been reported to show increased bacteriostatic effect on complexing with transition metal ions \(^176,177\). Extensive investigations of antibacterial activity of metal complexes of biologically active organic compounds have revealed an enhancement of their activity.
especially against *S. aureus* on complex formation\textsuperscript{178-182}.

The Schiff bases are well known for their biological activities\textsuperscript{183-185}. Antibacterial and antifungal activities of Schiff bases have been reported to increase on coordination with metal ions. The activities are invariably dependent on the structure and orientation of various moieties of chelates\textsuperscript{46,48,94,186-189}. The increased fungitoxicity is probably due to the faster diffusion of metal chelates as a whole through the cell membrane or due to the combined activity effect of the metal and ligand\textsuperscript{190}. The Schiff bases isatin-thiosemicarbazones and isatin-benzoxazole-2-hydrazone show increased antimicrobial activity against *S. aureus* when chelated with divalent metal ions; and Cu(II) chelates show the highest activity\textsuperscript{189,191}.

Metal complexes of aminoglycoside class of antibiotics [gentamycin or streptomycin complexes of Cu(II), Ni(II), Co(II) and Zn(II)] have been reported to be more bacteriostatic than the free antibiotics. It is assumed that the number of binding sites and the effect of chelation might be responsible for this increased activity of the complexes. The chelation reduces the polarity of metal ion and ligand which in turn increases the hydrophobic character of metal chelates. Hence the permeation mechanism through the lipid layer of microorganism becomes more effective causing an increase in the antibacterial activity of
The highest dilution of test metal chelate which inhibit the visual or detectable growth of test organism is generally called minimum inhibitory concentration (mic, \( \mu g \text{ ml}^{-1} \)). Shrivastava and coworkers have reported the spectral and antibacterial studies of metal complexes of schiff base derived from 2-furylglyoxal and 2-aminopyridine against bacteria Bacillus subtilis, Escherichia coli, S. aureus and S. veridine and mic of these complexes were estimated by disc diffusion method. Iron(III)chloride complexes of schiff bases of isoniazid with a number of carbonyl compounds have been screened for their antitubercular and antibacterial activities invitro. In the case of antitubercular study of complexes, the mic reported is nearly 1 \( \mu g \text{ ml}^{-1} \). However, the complexes having functional groups OH, OCH\(_3\), N(CH\(_3\))\(_2\) and CH=CH in the ligand exhibited higher activity than others (mic-0.5 \( \mu g \text{ ml}^{-1} \)). The complexes were found active against S. aureus and E. coli.

Thiols and their derivatives are potent bacteriostatic and fungitoxic compounds. N salicylidene-o-aminobenzenethiol and their metal complexes have been screened for their antibacterial activity against S. aureus and E. coli. The mic of various complexes are estimated by serial dilution method. All the Cu(II), Ni(II), Mn(II) and complexes.
Zn(II) complexes showed increased activity than the ligand, the most active being the Mn(II) complex.

L-Alanine forms schiff base with 4-hydroxysalicylaldehyde which exhibit carcinostatic effect. However, metal complexes of 4-hydroxysalicylidene L-alanine with Co(II), Cu(II) and Ni(II) are reported to show enhanced antitumour activity; Cu(II) complex being the most powerful. Furylidene and 5-nitrofurylidene benzoyl hydrazines are known potent fungicides. Fungitoxicity of their metal chelates was established to be in the order Cu > Ni > Fe > Zn > Mn > Co against *Rhizoclonia solani*.

The increase in the antimicrobial activity of organic compounds on complexing with metal ion has been established as a common phenomenon. However, reports concerned with the lowering of antibacterial activity of organic compounds on chelation are not rare. 2-Thienylglyoxal-4-iminobenzoic acid has been found to exhibit more antibacterial activity than its metal complexes when the ligand and complexes were screened against *S. aureus* by agar gel diffusion method. o-(N-pyrroldenimino)phenol and o-(N-thiophene-2-carbaldimine)benzoic acid have been found to be more active than their metal complexes against *B. subtilis* and *B. pumpliis*. Transition metal complexes of many ONS donors show lower antibacterial and antifungal activities compared to the respective ligands.
With a few exceptions, chelation of biologically active organic compounds with transition metal ions, has shown considerable increase in antimicrobial activity. An extensive and systematic research in this field may result in the emergence of newer metal complexes with specific bacteriostatic, fungitoxic, antitumour or tuberculostatic activity capable of overcoming the resistance of microorganism to common drugs and inhibiting the growth of pathogenic hospital isolates.

Present Investigation

The present thesis deals with the studies on metal complexes of some polydentate Schiff bases derived from isonicotinoylhydrazine, salicyloylhydrazine and o-aminothiophenol. In all, fifty seven new complexes of metal ions Cu(II), Ni(II), Co(II), Mn(II), Zn(II), Cd(II), Fe(III) Cr(III) and oxovanadium(IV) have been isolated in solid state and investigated. The Schiff bases prepared and used as ligands are N-(2-furylidene)N'-isonicotinoylhydrazine (FINH), N-(2-thienylidene)N'-isonicotinoylhydrazine (TINH), N-(2-furylidene)N'-salicyloylhydrazine (FSAH), N-(2-thienylidene)N'-salicyloylhydrazine (TSAH) and glyoxal bis-(2-mercaptoanil) (GBMA).

Chloride, perchlorate, nitrate, sulphate, acetate,
thiocyanate and benzoate ions are used as counter anions. The complexes have been characterised by elemental analysis and conductance and magnetic susceptibility measurements and infrared, electronic and ESR spectra. The nature of bonding has been established for four iron(III) complexes by studying their Mossbauer spectra at room temperature. The lattice constants of one of these complexes have been determined with the help of X-ray powder diffraction. Based on these investigations conclusions have been drawn regarding possible structure and nature of bonding in these complexes.

A few of the complexes have been screened for their antibacterial activity against the gram positive bacteria, Staphylococcus aureus by turbidimetric assay method.

Chapterwise arrangement of the thesis

A brief introduction to the coordination chemistry of Schiff bases, a short review on the complexes derived from various Schiff bases of isonicotinoylhydrazine, salicyloylhydrazine and o-aminothiophenol and a note on the antibacterial activity of metal complexes have been presented in chapter I. The scope of the present investigation and chapter wise arrangement of the thesis are also included in this chapter.
The details of the purity of the reagents used, preparation and characterisation of all the five ligands, analytical procedures and the apparatus used are given in chapter II. The method of antibacterial assay is also described in this chapter.

Chapter III deals with the preparation, characterisation and the antibacterial activity of some of the copper(II) complexes isolated using the schiff bases, FINH, TINH, FSAH, TSAH and GBMA. The studies on the isolation, structural elucidation and bacteriostatic effect of a few nickel(II) complexes of the five schiff bases have been presented in chapter IV. Seven new cobalt(II) complexes isolated with the five schiff bases mentioned above have been characterised and two of these complexes tested for their antistaphylococcal activity. These are discussed in chapter V.

The studies on the preparation, structure determination, Mossbauer spectra and antibacterial effect of a few iron(III) complexes with the ligands, TINH, FSAH, TSAH and GBMA are explained in chapter VI. A few oxovanadium(IV) complexes of the five schiff bases have been isolated and structure established. One of the complexes has been tested for the antibacterial activity and compared its activity with that of the free ligand. This is discussed in chapter VII.
Chapter VIII deals with the preparation and characterization of a few zinc(II) and cadmium(II) complexes with ligands FINH, FSAH and TSAH. A comparative study on the bacteriostatic effect of zinc(II) and cadmium(II) complexes of FINH is also presented in this chapter. The last chapter presents the isolation and characterisation of two complexes of manganese(II) and four complexes of chromium(III) ions.